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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,967	10/16/2006	Rakesh Kumar	PR60682USW	7447

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EXAMINER	
PAGONAKIS, ANNA	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
10/06/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/599,967	KUMAR ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/27/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets, 8/27/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 8/27/2008 has been received and entered into the present application.

Claims 15-17, 25 are pending. Accordingly, claims 1-14, 18-24 have been cancelled and claims 15-17, 25 are currently amended.

As reflected by the attached, completed copy form PTO/SB/08A (two pages total), the Examiner has considered the cited reference.

Applicant's arguments, filed 8/27/2008 have been fully considered. Rejections not reiterated from the previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-16 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

Applicant uses the phrases "salts, solvate or physiologically functional derivative." It is unclear to the examiner which derivatives are being claimed as the claims fail to provide any compounds of the instantly claimed subject matter. It is not clear from the claim language whether the compounds are corresponding to the structure of the instantly claimed "salts, solvate or physiologically functional derivative" or to the function is unclear.

Applicant's Remarks

Applicant alleges that the rejection is rendered moot given the deletion of the phrase "physiological functional derivative."

Response to Applicant's Arguments

Examiner contends that "solvates" were included in the Office Action mailed on 2/28/2008. Therefore the rejection is proper and is therefore maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-17 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boloor et al. (WO02/059110, provided by Applicant) and Ciardiello et al. (Expert. Opinoin Investig. Drugs 2002 Vol. 11(6): 755-768) in view of Rusnak et al (Molecular Therapeutics 2001, pages 85-94).

Boloor et al. teach novel pyrimaidineamines as inhibitors of VEGFR-2 kinase activity. Such pyrimaidineamines are useful in the treatment of disorders, including cancer, associated with inappropriate angiogensis (page 3 of specification). The reference teaches the compounds may be used to treat cancer and can be used in combination with other anticancer drugs, such as growth factor function inhibitors including inhibitors of hepatocyte growth factor, erb-B2, erb-B4 and epidermal growth factor receptor (EGFr).

Ciardiello et al. lists a variety of human cancers that express EGFR: non small cell lung carcinoma, colorectal, gastric, pancreatic (which is specifically noted to be resistant to treatment with EGFR is overexpressed), ovarian, prostate, breast head and neck, and kidney tumors (see Table 1, page 758). The reference also states that TGF-alpha and EGFR are overexpressed in the majority of human cancer types, including NSCLC, breast and neck cancer, gastric, prostate, bladder, ovarian, colorectal carcinomas, and glioblastomas (page 757).

Rusnak et al. teach that GW2016 (the elected compound of formula II) is a potent inhibitor of ErbB-2 and EGFR tyrosine receptor kinase domains (see: abstract; Table 1 structure on page 88). The reference teaches that OSI—774 (Tarceva) and ZD1839 (Iressa) are small molecule epidermal growth factor receptor-selective tyrosine kinase inhibitor (abstract). The reference teaches treatment of and growth inhibition in human tumor cells overexpressing ErbB-2 and/or EGFR in a variety of cancer types: head and neck, vulva, breast, lung and gastric (see abstract and Table 3, page 90). The reference also teaches in vivo xenograft experiments with head and neck cancer and breast cancer cells (see abstract page 93 and Figure 7).

Neither of the three reference teach the presence of instantly elected formula I. Given that Boloor et al. teach that pyrimaidineamines are capable of treatment of cancer, one of ordinary skill in the art would have been motivated to create a pyrimaidineamine with a reasonable expectation of success. Further, it would have been obvious to a person of ordinary skill in the art to treat cancer with the elected compound GW2016 (Rusnak) in combination with the compound of formula I since both are pyrimaidineamines and thus both are capable for treatment of cancer. One would have reasonable expectation of success having been taught in the art that the majority of cancers overexpress EGFR or ErbB2 (Ciardiello).

In light of such, it would have *been prima facie* obvious to one of ordinary skill in the art to employ pyrimaidineamine as the cancer compound. Such a person would have been motivated to do so because it, would have been reasonably expected that each of the compounds would have exerted the same or substantially anti-cancer effect as the elected compound of formula II specifically disclosed by Rusnak, without any appreciable loss of activity of the composition in achieving the disclosed therapeutic objective (i.e., treatment of ccancer), absent factual evidence to the contrary.

With respect to claims 16, 17 and 25 the determination of pharmaceutically acceptable salts, that have the optimum therapeutic index are well within the level of one having ordinary skill in the art. Accordingly, the artisan would have been motivated to determine optimum pharmaceutically acceptable salts in order to get maximum effects of the active agent. Moreover, a recitation of the intended use of the claimed invention would result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claims. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1067) and In re Otto 136 USPQ 458, 459 (CCPA 1963). Additionally, Suggestion, teaching or motivation does not have to be explicity and "may be found in any number of

sources, including common knowledge, the prior art as a whole or the nature of the problem itself", citing Dystar Textilfarben GMBH v. C.H. Patrick Ci., 464 F.3d 1356 (Fed. Cir. 2006). For these reasons, the selection of a known material based on its suitability for its intended use, in this case the compounds of formula I and II, support a prima facie obviousness determination in Sinclair & Carroll Co. v. International Corp., 325 US 327, 65 USPQ 297 (1945).

Applicant's Remarks

Applicant alleges that it is not possible to predict a priori which combinations will be beneficial to patients and provides several references and with different chemotherapeutic agents, to support this allegation. Applicant further states that these examples illustrate that while it might be obvious to try various anti-cancer agents in combination for the treatment of cancer, it is not possible to predict which particular combinations will offer therapeutic advantages in a particular type of cancer. Additionally, Applicant alleges to have overcome the obviousness rejection by providing the reference Slamon et al.

Response to Applicant's Arguments

Examiner contends that given both compounds are known to effectively treat breast cancer one of ordinary skill in the art would have been motivated to combine treatment. Examiner cites Applicant's own provided reference which states, "the rationale for combination chemotherapy is to use drugs that work on different parts of the cancer cell's life cycle" (Beers et al). Arguendo the above, Applicant has failed to provide a representative set of comparisons of similar types of agents in support of their argument. Applicant's representative have simply "pick and choose" different agents, many of which have varying mechanisms of actions from the agents claimed. Regarding, the Slamon et al. reference, Applicant have not set forth any reason why the results provided in fact render the invention unobvious.

Accordingly, there is no reason or basis advanced by Applicant to reasonably assume or infer that the invention is in fact unobvious, as a result, such an argument is unpersuasive.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614